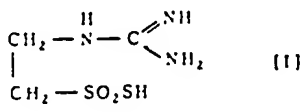
BY

87-140943/20 B05 SOUG- 02.10.85
SOUGO YAKKOU KK *J6 2081-365-A
02.10.85-JP-218009 (14.04.87) A61k-31/18 C07c-161
Guanidino ethane thiosulphonic acid cholesterol decreasing agent - prepd. by reacting guanidino ethane sulphinic acid with sulphur in presence of base
C87-058856

B(10-A9B, 12-G1A, 12-H3) 3
B0170

Guanidinoethanethiosulphonic acid of formula [I] is new:



[I]

USE/ADVANTAGE

[I] is useful as cholesterol decreasing agent.

The compound has strong cholesterol decreasing activity and strong HDL-cholesterol increasing activity without toxicity (LD_{50} = 3000 mg/Kg in the rat).

PREPARATION

Cpd. [I] is prepared by reacting hypotaurocyamine (guanidinoethanesulphinic acid) with sulphur in the presence of base.

Caustic alkali such as NaOH, KOH is used as base. Powdered sulphur is pref. used.

Solvent is pref. an alcohol such as MeOH, EtOH or i-PrOH.

ACTIVITY

Test results on male rats allowed to eat normal food, cholesterol food, and cholesterol food with [I] (200 mg/Kg. day) for 2 weeks [total] cholesterol in serum, HDL-cholesterol in serum, HDL-cholesterol (mg/dl)] are: 109.2, 48.5; 521.2, 20.5; 283.9, 28.1.

EXAMPLE

Hypotaurocyamine (0.18 mol) was dissolved in 0.2N NaOH. EtOH (1800 ml) and sulphur (6.3g) were added. The mixture was stirred under reflux until the sulphur completely disappeared and was allowed to stand overnight. Crude crystals were filtered and washed with CS_2 (twice) and EtOH. The crystals were dissolved in hot-water and recrystallized by adding EtOH (2700ml) and cooling. Filtration and washing with ether afforded 26.4 g (80.1%) of [I]. mp 206-210°C. (4ppW67LDDwgNo0/0).

JG2081365-A

87-140944/20 B03 TOST- 02.10.85
TOHYOH STAUFER CHEM *J6 2081-368-A
02.10.85-JP-219681 (14.04.87) C07d-205/08
Highly stereoselective synthesis of beta-lactam deriv. - by treating lithium enolate of organic ester with organic imine cpd. in polar solvent
C87-058857

B(7-D1) 1
B0171

β-Lactam derivs. are synthesized highly selectively by treating lithium enolate of organic ester with organic imine cpd. in polar solvent.

The organic imine cpd. may be an imine coordinated with trialkylaluminum. When the cpd. is used as imine, cis prod. may be synthesized with 100% stereoselectivity.

USE/ADVANTAGE

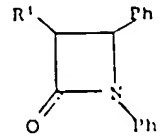
Lactams are formed with high stereoselectivity. Prods. are useful as pharmaceuticals.

EXAMPLE

n-BuLi (15% hexane soln.) (12 m mols.) was added to a soln. of diisopropylamine (12 m mols.) in n-hexane (7 ml) with ice-cooling under N_2, and resultant mixt. was stirred. n-Hexane was distilled off under reduced press., THF (5 ml) was added to the residue, and the mixt. was cooled to -78°C. $(CH_3)_2CHCH_2COOC_2H_5$ or $CH_3CH_2COOC_2H_5$ (10 m mols) was added within three minutes to the above mixt., and a soln. of $C_6H_5CH{=}NC_6H_5$ (10 m mols) in THF (5 ml) or a soln. of the imine (10 m mols) and AlR_3 (see below), (10 mmols) in THF (5 m mols) was added.

The low temp. cooling bath was removed and temp. of reaction mixt. was elevated slowly to room temp. over ten hours. The mixt. was then hydrolysed with 1N HCl aq. soln. and prod. was extracted with benzene to give β-lactam.

Yield of the β-lactam and results of cis : trans ratio are as follows:



(II)

(a) R^1 = i-Pr:

AlR_3	Yield (%)	Cis : trans ratio
None	87	0 : 100
$Al(CH_3)_3$	73	100 : 0
$Al(C_2H_5)_3$	75	100 : 0
Al i-Bu$_3$	40	100 : 0

(b) R = CH_3:

AlR_3	Yield (%)	Cis : trans ratio
None	92	0 : 100
$Al(CH_3)_3$	85	100 : 0
$Al(C_2H_5)_3$	83	100 : 0
Al i-Bu$_3$	52	100 : 0

(5ppW69EDDwgNo0/0).

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